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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,549	08/03/2001	Jeffrey C. Rapp	AVI013N	1388

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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM-

Office Action Summary	Application No.	Applicant(s)	
	09/922,549	RAPP, JEFFREY C.	
	Examiner	Art Unit	
	Gerald G Leffers Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *70-155* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *70-155* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/17/2004 has been entered.

In the amendment filed 5/17/2004 all of the pending claims were cancelled (claims 1-69) and new claims were added that are directed to isolated nucleic acids comprising a chicken lysozyme gene expression controlling region, or sequences with identity or the ability to hybridize thereto, operatively linked to a heterologous coding sequence (new claims 70-155). Claims 70-155 are pending and under consideration in the instant application.

Response to Amendment

Any rejection of record in the previous office action (mailed 1/29/2004) not addressed herein is withdrawn. In particular, applicants' argument that the metes and bounds of the term "intrinsically curved" DNA would be recognizable in the art is persuasive. Upon reviewing the prior art (e.g. applicants' submission of Spurio et al; EMBO Journal, Vol. 16, No. 7, pages 1795-1805, 1997), it is apparent that the term is merely broad and can be reasonably considered to encompass any nucleic acid that curves to *any* degree in the absence of DNA-binding proteins under *any* conditions. This is the interpretation of the term the examiner has used in interpreting new claims 70-155.

Claim Objections

Claim 82 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 82 specifies that the polyadenylation signal is "derived from" an SV40 virus. Claim 70 specifies that the entire DNA molecule be "obtained from a chicken". Thus, claim 82 specifies a further element that is not encompassed by the claim upon which it is dependent.

Claims 95, 146 & 154 are objected to because of the following informalities: the word "Isolated" is improperly capitalized in the middle of a sentence. Appropriate correction is required.

Claim 102 is objected to because of the following informalities: the phrase "...an isolated lysozyme gene expression controlling region...and controls expression of the nucleic acid..." is grammatically incorrect. Appropriate correction is required.

Claims 136-139 & 148 are objected to because of the following informalities: the cited claims encompass embodiments that were not elected by applicants in response to the original restriction requirement (i.e. cells found *in vivo*, such as those found in a transgenic animal). It would be remedial to amend the claims to specify an "isolated" cell. Appropriate correction is required.

Claims 140-147, 149-154 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is

required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The independent claims upon which these claims are dependent are all directed to a cell while these claims are all directed to nucleic acids. As such, the cited dependent claims do not further limit the cell that is claimed in the independent claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 70-155 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections, necessitated by applicants' amendment of the claims in the response filed 5/17/2004.**

Claim 70 is vague and indefinite in that the metes and bounds of the phrase "...wherein the DNA molecule is obtained from a chicken..." are unclear. The phrase is unclear in that the phrase appears to indicate that both the chicken lysozyme gene controlling region and the heterologous gene are obtained from a chicken (i.e. the heterologous gene encodes a polypeptide that is native to chickens). The instant specification, however, appears to be primarily directed to the expression of heterologous transgenes that are obtained from non-chicken sources (e.g. interferon). While it is true that chicken genes encoding polypeptides endogenous to chickens fall within the broad scope of polypeptides contemplated by the instant invention, it appears the cited phrase might be intended to specify that the lysozyme gene expression controlling region is

obtained from a chicken while allowing the operatively linked gene to be from any source. If this latter interpretation is correct, it would be remedial to amend the claim language to clearly indicate that it is the lysozyme gene expression controlling region that is obtained from a chicken (or is a chicken lysozyme gene expression controlling region).

Claim 70 is further vague and indefinite in that it is not clear that the term "obtained from a chicken" specifies that the DNA molecule is necessarily a native chicken sequence. Upon reading the specification, it appears the intended meaning of this phrase is that the DNA molecule is a native sequence. However, the claim as written could also reasonably be read to encompass nonnative DNA molecules recovered from chicken cells (e.g. a transgenic construct isolated from the tissue of a transgenic animal). It would be remedial to amend the claim language to clearly distinguish between the two possibilities.

Claim 88 recites a gene expression controlling region comprising "a" nucleotide sequence of SEQ ID NO: 67 or "a" complement of SEQ ID NO: 67. As written, the claim thus encompasses embodiments where the expression controlling region comprises only a single di-nucleotide sequence from SEQ ID NO: 67 or any di-nucleotide sequence complementary to SEQ ID NO: 67. This interpretation appears to be contrary to the description provided in the specification where it is "the" sequence of SEQ ID NO: 67 or "the" complement of SEQ ID NO: 67 that is described as the gene expression controlling region for the chicken lysozyme gene. If this latter interpretation is correct, it would be remedial to amend the claims to clearly indicate "the" sequence of SEQ ID NO: 67 or "the" complement of SEQ ID NO: 67.

Claims 88, 121 & 148 specify hybridization conditions where hybridization occurs in the presence of "about" 1.0 M Na ion and at a temperature of "about" 60°C. The term "about" is not

explicitly defined in the instant specification with regard to the parameters of molarity and temperature, leaving it up to the individual practitioner to subjectively decide what satisfies the limitations of "about" 1.0 M Na ion and of "about" 60°C.

Claim 96 is vague and indefinite in that there is no clear and positive prior antecedent basis for the phrase "The DNA molecule of Claim 95" in claim 95. It would be remedial to include the term "isolated" before the word "DNA".

There is no clear and positive prior antecedent basis for the term "the nucleic acid" in line 3 of claim 102.

Claims 140-146 all recite the term the "isolated" lysozyme gene expression controlling region of claim 136. There is no clear and positive prior antecedent basis for an "isolated" gene expression controlling region in claim 136.

Similarly, claim 147 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "the DNA molecule" in claim 146, upon which claim 147 is dependent.

Claims 149-154 all recite the term the "isolated" lysozyme gene expression controlling region of claim 148. There is no clear and positive prior antecedent basis for an "isolated" gene expression controlling region in claim 148.

Similarly, claim 155 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term "the DNA molecule" in claim 154, upon which claim 155 is dependent.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 70-87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection, necessitated by applicants' amendment of the claims in the response filed 5/17/2004. This is a NEW MATTER rejection.**

Each of the claims is directed to an isolated DNA molecule comprising a lysozyme gene expression controlling region operably linked to a nucleic acid molecule encoding a polypeptide other than a chicken lysozyme protein wherein the DNA molecule is obtained from a chicken and directs expression of the nucleic acid in a cell. As written the claims are directed to a genus of DNA molecules wherein the lysozyme gene expression controlling region is necessarily linked to heterologous coding sequence encoding chicken polypeptides other than chicken lysozyme. There is no literal support in the specification as originally filed for claiming this particular genus of DNA molecules encoding only chicken polypeptides. Therefore, claim 70 and dependent claims comprise impermissible new matter.

Claims 70-71, 75-103, 106-137, 140- rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the

claimed invention. **This is a new rejection, necessitated by applicants' amendment of the claims in the response filed 5/17/2004. This rejection is written on the grounds of an insufficient description of specific embodiments of the recited lysozyme gene expression controlling region to describe the broadly claimed genus of such expression control elements**.

Claim 70 is directed to an isolated DNA molecule comprising a lysozyme gene expression controlling region operably linked to a nucleic acid molecule encoding a polypeptide other than a chicken lysozyme protein wherein the DNA molecule is obtained from a chicken and directs expression of the nucleic acid in a cell. As such it reads on *any* variant of a lysozyme gene expression control region of *any* size obtained from *any* chicken species which must retain the functional activity of regulating the expression of the operatively linked coding sequence.

Claim 102 is directed to an expression vector comprising an isolated lysozyme gene expression controlling region wherein the lysozyme gene expression controlling region is obtained from a chicken. Likewise, claim 136 is directed to a cell comprising a lysozyme gene expression controlling region wherein the lysozyme gene expression controlling region is obtained from a chicken. These claims also read on any variant of a lysozyme gene expression control region of any size obtained from any chicken species that must also retained the functional activity of regulating the expression of the operatively linked coding sequence.

Claims 88, 121 & 148 each specify that the lysozyme gene expression controlling region has some sort of relationship with the embodiment disclosed by the instant specification (SEQ ID NO: 67). However, the degree of relationship is not limiting to any significant degree. For example, claims 88, 121 & 148 do not specify that the region is obtained from chicken species.

Also, the claims specify a lysozyme gene expression controlling region comprising "a" nucleotide sequence of SEQ ID NO: 67 or "a" complement of SEQ ID NO: 67. As written, the claims thus encompass embodiments where the expression controlling region comprises only a single di-nucleotide sequence from SEQ ID NO: 67 or any di-nucleotide sequence complementary to SEQ ID NO: 67. Further, claims 88, 121 & 148 specify hybridization conditions where hybridization occurs in the presence of "about" 1.0 M Na ion and at a temperature of "about" 60°C. The term "about" is not explicitly defined in the instant specification with regard to the parameters of molarity and temperature, leaving it up to the individual practitioner to subjectively decide what satisfies the limitations of "about" 1.0 M Na ion and of "about" 60°C. As such, the claims read on *any* nucleic acid comprising promoter activity that can hybridize to SEQ ID NO: 67 under *any* conditions. Thus, claims 88, 121 & 148 read on an enormous genus of gene expression controlling regions that must meet the functional limitations of the rejected claims.

Finally, several of the claims specify that the gene expression control region has at least 75% identity to SEQ ID NO: 67. While these claims specify some specific degree of identity to the ~12 kb expression control region exemplified by the instant specification, these claims still encompass a broad genus of such control elements where ~3000 nucleotides within the ~12,000 nucleotide sequence of SEQ ID NO: 67 can be changed and the nucleic acid must retain functional activity (e.g. where only a relative few of the 3000 nucleotides are contiguous with one another).

With regard to claims that specify that the gene expression control region is obtained from chicken, the instant specification and prior art do not teach the degree of conservation of

the chicken lysozyme gene expression control region described in the instant specification (SEQ ID NO: 67 obtained from *Gallus gallus*) across different chicken species. This makes it unpredictable as to whether one could reliably extrapolate from the teachings of the instant specification and prior art concerning the structural/functional characteristics of SEQ ID NO: 67 to lysozyme gene expression control regions obtained from other species. The instant specification does provide some degree of prophetic guidance based on BLAST analysis of SEQ ID NO: 67 as to what regulatory elements are located within SEQ ID NO: 67 (e.g. page 65, Table II). However, there is no significant discussion of what specific regions can be modified and still retain activity. For example, there is no discussion of what combinations of the different elements of SEQ ID NO: 67 can be made to construct a gene expression control region that meets the functional limitations of the claims where the control region is not directly obtained from a chicken.

Given the extraordinary breadth of control regions encompassed by the rejected claims, and given the lack of significant guidance regarding those embodiments that comprise <75% identity to SEQ ID NO: 67, the skilled artisan would not have been able to envision a sufficient number of specific embodiments to describe the broadly claimed genus of gene expression control regions. Therefore, the skilled artisan would reasonably have concluded applicants were not in possession of the recited invention for the rejected claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 70, 74-76, 80, 83-90, 94-95, 97-102, 106-109, 113-114, 116-124, 128-134, 136, 140-146, 148-154 are rejected under 35 U.S.C. 102(b) as being anticipated by Stief et al (reference T on applicants' submission; Nature, Vol. 341, pages 343-345, 1989; see the entire reference). **This is a new rejection, necessitated by applicants' amendment of the claims in the response filed 5/17/2004.**

Stief et al teach a series of reporter constructs comprising various elements of the chicken lysozyme gene expression control region operatively linked to a chloramphenicol acetyl transferase coding sequence (CAT) (e.g. Figure 1). These regulatory sequences included an enhancer domain ($^{-}$6.331 to $^{-}$5.772 kb), the promoter element ($^{-}$579 to $^{+}$15 nucleotides) and two lysozyme gene 5' A elements ($^{-}$11.7 to $^{-}$8.7 kb). These constructs directed expression of the operatively linked CAT sequence in HD11/HBC1 cells upon transfection and integration of the constructs into the cells (e.g. Figures 2-3).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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